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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/517,466	03/02/2000	James L. Hartley	0942.4680003/RWE/BJD	4289
26111	7590	11/18/2005	EXAMINER	
STERNE, KESSLER, GOLDSTEIN & FOX PLLC 1100 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005			JOHANNSEN, DIANA B	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 11/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/517,466	HARTLEY ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-56 is/are pending in the application.
- 4a) Of the above claim(s) 50-56 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>0105a-b;0205a-b</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 39-49, and of sequence (a) in claim 39, in the reply filed on July 28, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 50-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Additionally, claims 39-49 to the extent that they are drawn to non-elected sequences (b)-(f) of claim 39 are also withdrawn from consideration as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 28, 2005.

Information Disclosure Statement

3. The "Eighth Supplemental" information disclosure statement filed January 21, 2005 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of foreign patent documents AL20 and AM20, which are not in the English language. These two documents have been placed in the application file, but the information referred to therein has not been considered. It is noted that the examiner has considered document AS213, which is identified by applicant as an English language abstract of documents AL20 and AM20.

Art Unit: 1634

4. Regarding the "Ninth Supplemental" information disclosure statement filed February 9, 2005, the citations for documents AR215, AS215, AT215, and AR216 have not been initialed because the numbers of these unpublished applications will not be printed on the face of an issued patent. However, it is noted that the examiner reviewed these application files on October 31, 2005.

Claim Rejections - 35 USC § 112, indefiniteness, and the language of claim 49

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 49 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 is indefinite over the recitation "the isolated nucleic acid molecules of claim 39." It is noted that claim 39 refers to several different isolated nucleic acid molecules in the alternative, not as a group. It is not clear whether claim 49 encompasses a host cell comprising a single recited sequence, or whether the claim requires a cell comprising all the isolated nucleic acids of claim 39. Accordingly, the scope of the claim is not clear.

With further regard to claim 49, it is noted that the discussion of "isolated" nucleic acids at pages 58-59 of the specification indicates that this language may encompass molecules "maintained in heterologous host cells." Accordingly, the use of the term "isolated" in claim 49 does not render the claim indefinite.

Art Unit: 1634

Furthermore, while the claim is drawn to a "host cell" (rather than an "isolated host cell"), the specification (in addition to the above) discloses that the sequence of (a) (see claim 39) was produced by mutagenesis, and the examiner's search of the prior art did not identify any naturally occurring molecule meeting the structural requirements of the claims. Accordingly, claim 49 is drawn to statutory subject matter.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 39-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acid molecules comprising SEQ ID NO: 87 (including the molecule disclosed by applicant as SEQ ID NO: 60), does not reasonably provide enablement for any isolated nucleic acid molecule comprising the nucleotide sequence of (a) of claim 39 "located within a recombination site." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level

Art Unit: 1634

of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

The claims are to drawn isolated nucleic acid molecules comprising the nucleotide sequence ATTATAC located "within a recombination site" (see claim 39), as well as various vectors and host cells comprising the nucleic acid molecule. It is noted that the specification states that recombination sites "are discrete sections or segments of DNA on the participating nucleic acid molecules that are recognized and bound by the recombination proteins (p. 5)/a site-specific recombination protein (p. 33) during the initial stages of integration or recombination" (see pages 5 and 33 of the specification). Thus, the term "recombination site" as used in the specification is consistent with the art-recognized meaning of this terminology, and encompasses any sequence recognized and bound by recombination proteins during integration and/or recombination. Accordingly, the instant claims are sufficiently broad so as to encompass molecules comprising the sequence ATTATAC located within any type of recombination site.

It is unpredictable as to whether one of skill in the art could make and use applicant's invention in a manner reasonably commensurate with the claims. The specification provides evidence that the mutation of the first nucleotide of the 7 base pair overlap of the attL recombination site 15 base pair core region from T to A (such that the 7 base pair sequence changes from ITTATAC to ATTATAC) results in

Art Unit: 1634

increased recombination efficiency (see Examples 21 and 22, and SEQ ID Nos 60 and 87 in particular). Accordingly, one of skill in the art could clearly prepare nucleic acids comprising such mutated attL sequences and use said nucleic acids in various methods requiring site-specific recombination. However, the specification is silent with regard to other att recombination sites comprising this particular mutated sequence, and with regard to what effect this mutation would have (if any) on recombination using such sequences. Further, the specification does not disclose the use of molecules comprising this 7 base pair sequence located in any type of non-att recombination site/sequence. Thus, while the specification enables the use of one particular type of nucleic acid molecule encompassed by the claims, the vast majority of molecules encompassed by the instant claims are neither not enabled by the teachings of applicant's specification. Given the high level of skill of one skilled in the relevant art, it is clearly within the ability of such a practitioner to synthesize a variety of molecules encompassed by the claims and to, e.g., assay those molecules to determine whether any of them are useful in recombination. However, the outcome of such experimentation cannot be predicted, and therefore it is completely unpredictable as to whether such additional molecules could be successfully used in a manner analogous to the particular attL mutant sequence employed by applicant. Lacking guidance from the specification, one skilled in the art may look to the teachings of the prior art for further guidance and enablement of a claimed invention. However, in the instant case, the prior art does not disclose other molecules meeting the requirements of the claims. The closest prior art reference, Zucman-Rossi et al (Proc. Natl. Acad. Sci. USA

Art Unit: 1634

95:11786-11791 [9/1998]) discloses a sequence comprising a breakpoint region (EWSR1) that includes the sequence ATTATAC (see entire reference, particular page 11786 and Figure 1, as well as the sequence disclosed in GenBank Accession No. Y08806, in which ATTATAC is located, e.g., within intron 8 at nucleotide 38969). However, the sequence ATTATAC in the molecule of Zucman-Rossi et al is not located within a "recombination site" as required by the instant claims – the site flanking ATTATAC in the molecule does not correspond to that of a known recombination site, and Zucman-Rossi et al do not disclose that this particular site is a breakpoint or that recombination proteins bind this site, etc. Accordingly, the teachings of the prior art cannot be relied upon for enablement of additional molecules encompassed by applicant's claims. Thus, given the lack of sufficient guidance provided by the specification and the prior art, it would require undue experimentation to make and use applicant's invention in a manner reasonably commensurate with the instant claims.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1634

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Diana B. Johannsen
Primary Examiner
Art Unit 1634
November 10, 2005